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OPSONIC REACTIVATION OF ANTIPNEUMOCOCCUS SERUM

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Mennes[1] first noted that the serum of animals immunized against pneumococci contains substances that favor phagocytosis of virulent pneumococci. Wright and Douglas[2] described as opsonins substances in normal serum that attach themselves to bacteria and prepare them for phagocytosis. Neufeld[3] showed that immune serum may alter bacteria so that they become susceptible to phagocytosis, and he called the substances responsible for this change bacteriotropins. According to Hektoen,[4] there appears to be no fundamental difference between opsonins and bacteriotropins; normal serum contains a variety of opsonic substances each of which is specific for a given bacterium, and in immune serum the specific opsonic substance for the particular bacterium or cell with which immunization has been produced is developed in a high degree; in both cases the full effect is produced by the interaction of two substances, one of which is destroyed by heating, while the other remains unaffected; the latter is opsonic in itself but its action is enhanced by the heat sensitive element, and it is the heat resistant element that is produced specifically by experimental immunization or as the outcome of spontaneous infection. Clough[5] found that soon after the crisis in pneumonia and also after lysis, the serum may be actively opsonic for highly virulent homologous pneumococcus. He states[6] that when the serum of patients recovering from pneumonia "became inactive or feeble as a result of overheating or dilution, the phagocytic activity could not be restored or increased by the addition of complement."

The purpose of my experiments was to study once more the opsonic activity of antipneumococcus serum with special reference to this problem of reactivation.

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[1] Ztschr. f. Hyg. u. Infectionskrankh., 1897, 25, p. 413.

[2] Proc. Royal Soc., 1903, 72, p. 857.

[3] Deut. Med. Wchnschr., 1904, 30, p. 1458.

[4] Jour. Am. Med. Assn., 1914, 62, p. 254.

[5] Bull. Johns Hopkins Hosp., 1913, 24, p. 295.

[6] Ibid., 1919, 30, p. 167.

The pneumococci used in the experiments were obtained from the Army Medical School. The types 1, 2 and 3 strains are virulent, about one ten millionth c c of an 18-hour broth culture killing mice within 48 hours. The type 4 strain (74), also from the Army Medical School, was derived from a case of influenza pneumonia. The cultures were transferred on blood-agar slants every third or fourth day. For the experiments a 24-hour growth in 0.2% glucose broth was used.

Antipneumococcus serum of types 1, 2 and 3 was also obtained from the Army Medical School. The type 4 serum was the serum of a rabbit immunized against strain 74. Serum from six cases of lobar pneumonia was studied also, blood being drawn from the vein at the elbow 4-6 days after crisis. In one case (patient 2) blood was withdrawn the first day after the crisis.

Human leukocytes were used: About 1 c c of blood was taken from the lobe of the ear of a normal person and mixed with 2% solution of sodium citrate; after centrifugation and washing with 0.85% salt solution, the leukocytic layer was removed and suspended in salt solution. Fresh normal human serum was obtained in the usual way.

The opsonic activity of the serums was determined by mixing serum, salt solution, leukocytes and bacterial suspension in capillary pipets, which were incubated for 30 minutes at 37 C., smears made, and stained with carbol thionin. The degree of phagocytosis was estimated by counting the number of leukocytes per 100 that showed phagocytosis and also the number of pneumococci ingested by each leukocyte. In the activation experiments, the same process was followed except that about 0.01 c c of the fresh (activating) serum was added to the mixture, the amount of salt solution being reduced accordingly.

Pneumococcus type 1 proved resistant to phagocytosis with fresh normal human serum, the greatest number of leukocytes showing phagocytosis in any one specimen being 8 per 100 and the average number of bacteria in each phagocytic leukocyte being 2. Pneumococcus 2 also was resistant to phagocytosis with fresh normal human serum, the greatest number of leukocytes showing phagocytosis in any one experiment being 3 in 100. Pneumococcus types 3 and 4 were more readily phagocyted under the influence of fresh normal human serum than the strains of types 1 and 2.

Antipneumococcus serums types 1, 2 and 3 were found to have only slight opsonic action on the homologous pneumococci, being even less active than fresh normal human serum. This was particularly true of serum 3. Serum 4 was actively opsonic for pneumococcus 4. Although the opsonic activity of serums 1, 2 and 3 was very slight, agglutination occurred in all the preparations, and in pneumococci tended to group themselves about the leukocytes.

The failure of the antipneumonic serum to opsonize homologous pneumococci may be explained by the absence of the thermolabile, complement-like element, and in that case the addition of fresh normal human serum should result in an increase in phagocytosis of the pneumococci. Accordingly, a number of activation experiments were made and, as shown in table 1, a marked increase in the action of antipneumonic serum, type 1, for the homologous pneumococcus resulted after the addition of a minute quantity of fresh normal serum. Serums 2 and 3 failed to show any increase in opsonic activity, after the addition of fresh normal human serum; serum 4, while relatively active, was distinctly enhanced in action by the addition of normal serum.

TABLE 1
REACTIVATION OF ANTIPNEUMOCOCCUS SERUM, TYPE 1

Antipneumococcus Serum	Pneumococci (Broth Culture)	Leukocytic Suspension	Normal Human Serum	Salt Solution	Results	
					Percentage of Phagocytic Leukocytes	Number of Pneumococci per Active Phagocyte
0.1	0.1	0.1	—	0.1	8	2
0.1	0.1	0.1	0.01	0.09	44	4
0.01	0.1	0.1	0.1	0.09	47	5
0.01	0.1	0.1	—	0.19	6	1
—	0.1	0.1	0.01	0.19	5	1
—	0.1	0.1	0.1	0.1	4	1

TABLE 2
REACTIVATION OF HEATED POSTCRITICAL PNEUMONIA SERUM FROM PATIENT 3

Antipneumococcus Serum	Pneumococci (Broth Culture)	Leukocytic Suspension	Normal Human Serum	Salt Solution	Results	
					Percentage of Phagocytic Leukocytes	Number of Pneumococci per Active Phagocyte
0.1 unheated	0.1	0.1	—	0.1	50	4
0.1 heated	0.1	0.1	—	0.1	1	4
0.1 heated	0.1	0.1	0.01	0.19	36	6
0.01 heated	0.1	0.1	0.1	0.09	12	3
—	0.1	0.1	0.1	0.1	4	1

Pneumococcus, types 1 and 3 already described, were used to determine the opsonic activity of serums of 6 pneumonia patients after crisis. Of the 6 serums, 5 proved to be actively opsonic and agglutinative for pneumococcus type 1, but not for type 3. The serum of patient 2 failed to cause phagocytosis of either type 1 or 3. The occurrence of such distinct agglutination and phagocytosis of pneumococcus type 1 suggests that it concerned a type 1 infection in 5 of the cases.

The serums were heated for 30 minutes at 56 C., and the opsonic power was greatly reduced thereby, but on the addition of a small quantity of fresh normal serum to the heated serum, the opsonic activity was restored almost to its original strength, as illustrated in table 2.

SUMARY AND CONCLUSION

The results show that the opsonic power of the samples studied of antipneumococcus serum of types 1 and 4 was increased by the addition of a minute quantity of fresh normal human serum; that serum from 5 patients with lobar pneumonia after crisis was actively opsonic for a pneumococcus strain of type 1, but lost this power in large measure on being heated to 56 C., regaining it, however, almost wholly by the addition of small quantities of fresh normal human serum in itself but feebly opsonic. The conclusion is that opsonin in antipneumococcus serum can be reactivated.